

AMENDMENTS TO THE CLAIMS

The present amendment amends claims 14, 15, 17, 18, 106 and 108 and adds claims 118-132. According to 37 C.F.R. § 1.121(c), after entry of the present amendment, the following claims are in the case:

1. (Previously Presented) A composition comprising at least a first nucleic acid segment in association with a structural matrix, wherein:
 - (a) at least a portion of said structural matrix is comprised of a porous, synthetic polymer that contains pores formed by gas foaming and pores formed by leaching out of a particulate from the polymer; or
 - (b) at least a portion of said structural matrix is a porous, modified alginate matrix that comprises at least one alginate chain section bonded to at least one molecule that mediates cellular interactions.
2. (Previously Presented) The composition of claim 1, wherein at least a portion of said structural matrix is comprised of a porous, synthetic polymer that contains pores formed by gas foaming and pores formed by leaching out of a particulate from the polymer.
3. (Previously Presented) The composition of claim 2, wherein at least a portion of said structural matrix is comprised of a porous, synthetic polymer that has an open pore structure.
4. (Previously Presented) The composition of claim 3, wherein at least a portion of said structural matrix is comprised of a porous, synthetic polymer that has an interconnected pore structure.

5. (Previously Presented) The composition of claim 2, wherein said structural matrix consists essentially of a porous, synthetic polymer that has an open pore structure.
6. (Previously Presented) The composition of claim 2, wherein said structural matrix comprises at least a first matrix portion comprised of said porous, synthetic polymer integrally connected to at least a second matrix portion comprised of an impermeable polymer.
7. (Previously Presented) The composition of claim 6, wherein said at least a first matrix portion is comprised of a porous, synthetic polymeric material that has a substantially uniform open pore structure, and wherein said at least a second matrix portion is comprised of the same synthetic polymeric material in a form that lacks an open pore structure.
8. (Original) The composition of claim 2, wherein said structural matrix is a biocompatible matrix.
9. (Original) The composition of claim 2, wherein said structural matrix is a biodegradable matrix.
10. (Original) The composition of claim 2, wherein said structural matrix is a biocompatible and biodegradable matrix.

11. (Original) The composition of claim 2, wherein at least a portion of said structural matrix is comprised of a lactic acid polymer, glycolic acid polymer or lactic acid/glycolic acid copolymer matrix.
12. (Original) The composition of claim 11, wherein at least a portion of said structural matrix is comprised of a lactic acid/glycolic acid (PLGA) copolymer matrix.
13. (Previously Presented) The composition of claim 1, wherein at least a portion of said structural matrix is a porous, modified alginate matrix that comprises at least one alginate chain section bonded to at least one molecule that mediates cellular interactions.
14. (Currently Amended) The composition of claim ~~13~~ 48, wherein at least a portion of said structural matrix is a modified alginate matrix that comprises at least one alginate chain section bonded to at least one molecule that mediates cellular interactions utilizing one or more uronic acid residues on said alginate chain section.
15. (Currently Amended) The composition of claim ~~13~~ 48, wherein at least a portion of said structural matrix is a modified alginate matrix that comprises at least one alginate chain section bonded to at least one cellular interaction molecule selected from the group consisting of cell adhesion molecules, cell attachment peptides, proteoglycan attachment peptide sequences, proteoglycans, cell adhesion polysaccharides, growth factors and cell adhesion enzymes.
16. (Original) The composition of claim 15, wherein at least a portion of said structural matrix is a modified alginate matrix that comprises at least one alginate chain section bonded to

at least one cellular interaction molecule selected from the group consisting of an RGD peptide, fibronectin, vitronectin, Laminin A, Laminin B1, Laminin B2, collagen 1 and thrombospondin.

17. (Currently Amended) The composition of claim ~~43~~ 48, wherein at least a portion of said structural matrix is a modified alginate matrix prepared by a method comprising:

- (a) providing a solution of a hydrogel-forming material and a surfactant;
- (b) mixing said solution in the presence of a gas to form a stable foam;
- (c) exposing said stable foam to conditions or agents that result in gelling of the hydrogel-forming material and in the generation of gas bubbles therein; and
- (d) exposing the hydrogel containing gas bubbles to a vacuum to release the gas and form the hydrogel material having macroporous open pore porosity.

18. (Currently Amended) The composition of claim ~~43~~ 48, wherein at least a portion of said structural matrix is a modified alginate matrix prepared by a method comprising:

- (a) providing a solution of a hydrogel-forming material, a surfactant and a gas-generating component, wherein said solution is capable of being mixed in the presence of a gas to incorporate the gas in the solution and form a stable foam;
- (b) mixing said solution in the presence of a gas to form a stable foam;
- (c) exposing said stable foam to conditions or agents that result in gelling of the hydrogel-forming material and to conditions or agents that result in generation of gas from the gas-generating component, to form a hydrogel containing gas bubbles therein; and
- (d) exposing said hydrogel containing gas bubbles therein to a vacuum to release the gas and to form the hydrogel material having macroporous open pore porosity.

19. (Original) The composition of claim 1, wherein said nucleic acid segment is a DNA molecule.
20. (Original) The composition of claim 1, wherein said nucleic acid segment is an antisense nucleic acid molecule or a ribozyme.
21. (Original) The composition of claim 1, wherein said nucleic acid segment is comprised within a plasmid or a recombinant expression vector.
22. (Original) The composition of claim 21, wherein said nucleic acid segment is operatively positioned downstream from a promoter within a recombinant viral expression vector.
23. (Original) The composition of claim 22, wherein said nucleic acid segment is operatively positioned downstream from a promoter within a recombinant adenovirus, a recombinant adeno-associated virus (AAV) or a recombinant retrovirus.
24. (Original) The composition of claim 21, wherein said nucleic acid segment encodes a protein or polypeptide.
25. (Original) The composition of claim 24, wherein said nucleic acid segment encodes a marker protein.

26. (Original) The composition of claim 24, wherein said nucleic acid segment encodes a protein or polypeptide that stimulates a bone progenitor cell when expressed in said cell.
27. (Original) The composition of claim 24, wherein said nucleic acid segment encodes a protein or polypeptide that stimulates a wound healing fibroblast, granulation tissue fibroblast or repair cell when expressed in said cell.
28. (Original) The composition of claim 24, wherein said nucleic acid segment encodes an antigenic or immunogenic protein or polypeptide that stimulates an immune response when expressed by an antigen presenting cell.
29. (Original) The composition of claim 24, wherein said nucleic acid segment encodes a cytotoxic or apoptosis-inducing protein or polypeptide that induces cell death upon expression in a cell.
30. (Original) The composition of claim 24, wherein said nucleic acid segment encodes a transcription or elongation factor, cell cycle control protein, kinase, phosphatase, DNA repair protein, oncogene, tumor suppressor, angiogenic protein, anti-angiogenic protein, immune response stimulating protein, cell surface receptor, accessory signaling molecule, transport protein, enzyme, anti-bacterial or anti-viral protein or polypeptide.
31. (Original) The composition of claim 24, wherein said nucleic acid segment encodes a hormone, neurotransmitter, growth factor, growth factor receptor, interferon, interleukin, chemokine, cytokine, colony stimulating factor or chemotactic factor protein or polypeptide.

32. (Original) The composition of claim 31, wherein said nucleic acid segment encodes a growth hormone (GH) protein or polypeptide, a parathyroid hormone (PTH) protein or polypeptide, a PTH1-34 polypeptide or a bone morphogenetic protein (BMP) protein or polypeptide.

33. (Original) The composition of claim 32, wherein said nucleic acid segment encodes a BMP-2A, BMP-2B, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7 or BMP-8 protein or polypeptide.

34. (Original) The composition of claim 31, wherein said nucleic acid segment encodes a transforming growth factor- α (TGF- α), TGF- β 1 or TGF- β 2 protein or polypeptide, a latent TGF β binding protein (LTBP) protein or polypeptide, an activin/inhibin protein or polypeptide, a fibroblast growth factor (FGF), a granulocyte/macrophage colony stimulating factor (GMCSF), an epidermal growth factor (EGF), a platelet derived growth factor (PDGF), an insulin-like growth factor (IGF) or a leukemia inhibitory factor (LIF).

35. (Original) The composition of claim 24, wherein said nucleic acid segment encodes a human protein or polypeptide.

36. (Original) The composition of claim 1, comprising at least a first and second nucleic acid segment.

37. (Original) The composition of claim 1, comprising a plurality of nucleic acid segments.

38. (Original) The composition of claim 1, further comprising a population of cells.
39. (Original) The composition of claim 38, wherein at least a portion of said nucleic acid segment is taken up by the cells comprised within said composition.
40. (Original) The composition of claim 1, prepared by admixing at least a first nucleic acid segment with said structural matrix.
41. (Previously Presented) The composition of claim 2, prepared by a process that comprises leaching out the particulate material from a composition comprising a gas foamed, synthetic polymeric material, at least a first nucleic acid segment and a leachable particulate material.
42. (Previously Presented) The composition of claim 2, prepared by a process that comprises the steps of:
- (a) preparing an admixture comprising at least a first nucleic acid segment, particles capable of forming a synthetic polymeric structure and a leachable particulate material;
 - (b) subjecting said admixture to a gas foaming process to create a porous, synthetic polymeric structure that comprises said at least a first nucleic acid segment and said leachable particulate material; and
 - (c) subjecting said porous, synthetic polymeric structure to a leaching process that removes said leachable particulate material from said porous, synthetic polymeric structure, thereby producing a synthetic polymeric structure of additional porosity that comprises said at least a first nucleic acid segment.

43. (Previously Presented) The composition of claim 42, wherein said admixture comprises said at least a first nucleic acid segment, beads or microspheres capable of forming a synthetic polymeric structure and said leachable particulate material.
44. (Original) The composition of claim 43, wherein said at least a first nucleic acid segment is incorporated within said beads or microspheres prior to said admixing or gas foaming steps.
45. (Previously Presented) The composition of claim 42, wherein said leaching process is conducted *in vitro* by subjecting said porous, synthetic polymeric material to a leaching agent.
46. (Previously Presented) The composition of claim 42, wherein said leaching process is conducted *in vivo* by exposing said porous, synthetic polymeric material to body fluids.
47. (Previously Presented) A composition comprising at least a first nucleic acid segment in non-covalent association with a structural matrix, wherein at least a portion of said structural matrix is comprised of a porous, synthetic polymer that contains pores formed by gas foaming and pores formed by leaching out of a particulate from the polymer.
48. (Previously Presented) A composition comprising at least a first nucleic acid segment in non-covalent association with a structural, porous modified alginate matrix that comprises at least one alginate chain section bonded to at least one molecule that mediates cellular interactions.

49. (Previously Presented) A composition comprising at least a first nucleic acid segment in association with a structural matrix, said structural matrix comprising at least a first matrix portion comprised of a porous, synthetic polymer that contains pores formed by gas foaming and pores formed by leaching out of a particulate from the polymer, wherein said first matrix portion is integrally connected to a second matrix portion comprised of an impermeable polymer.

50. (Previously Presented) The composition of claim 49, wherein said first and second matrix portions are comprised of the same synthetic polymeric material, separately fabricated to form a first, porous, synthetic polymer having a uniform open pore structure and a second, impermeable synthetic polymer lacking an open pore structure.

51. (Previously Presented) The composition of claim 49, wherein said first and second matrix portions are comprised of different synthetic polymeric materials.

52. (Original) An admixture, comprising at least a first nucleic acid segment; beads or microspheres of a polymer capable of forming a gas-foamed polymeric structure; and a leachable particulate material.

53. (Original) The admixture of claim **Error! Reference source not found.**, wherein said at least a first nucleic acid segment is incorporated within said beads or microspheres.

54. (Original) A method for making a structural matrix-nucleic acid composition, comprising providing at least a first nucleic acid segment to a structural matrix, wherein at least a portion of

said structural matrix is comprised of a porous polymer that contains pores formed by gas foaming and pores formed by leaching out of a particulate from the polymer.

55. (Original) The method of claim 54, comprising leaching out the particulate material from a composition comprising a gas foamed polymeric material, at least a first nucleic acid segment and a leachable particulate material.

56. (Original) The method of claim 55, comprising the steps of:

- (a) preparing an admixture comprising at least a first nucleic acid segment, particles of a polymeric material capable of forming a gas foamed polymeric structure and a leachable particulate material;
- (b) subjecting said admixture to a gas foaming process to create a porous polymeric structure that comprises said at least a first nucleic acid segment and said leachable particulate material; and
- (c) subjecting said porous polymeric structure to a leaching process that removes said leachable particulate material from said porous polymeric structure, thereby producing a polymeric structure of additional porosity that comprises said at least a first nucleic acid segment.

57. (Original) The method of claim 56, wherein said admixture is prepared by first incorporating said at least a first nucleic acid segment within said particles of a polymeric material and then admixing with said leachable particulate material.

58. (Original) The method of claim 57, wherein said admixture is prepared by first incorporating said at least a first nucleic acid segment within polymer beads or microspheres and then admixing with said leachable particulate material.

59. (Original) The method of claim 56, wherein the gas foaming process of step (b) comprises subjecting said admixture to an elevated pressure atmosphere of an inert gas in a manner effective to dissolve said gas into said polymeric material, and subjecting the gas-dissolved polymeric material to thermodynamic instability in a manner effective to cause nucleation and growth of gas pores sufficient to produce a continuous matrix of polymeric material that comprises said at least a first nucleic acid segment and said leachable particulate material.

60. (Original) The method of claim 59, wherein said thermodynamic instability is created by reducing said elevated pressure atmosphere.

61. (Original) The method of claim 56, wherein said leachable particulate material is a water-soluble leachable particulate material.

62. (Original) The method of claim 61, wherein said leachable particulate material is a salt, sugar or sugar alcohol.

63. (Original) The method of claim 62, wherein said leachable particulate material is NaCl, trehalose, glucose, sucrose or mannitol.

64. (Original) The method of claim 56, wherein said leaching process is conducted *in vitro* by contacting said porous polymeric material with a leaching agent.

65. (Original) The method of claim 56, wherein said leaching process is conducted *in vivo* by exposing said porous polymeric material to body fluids.

66. (Previously Presented) A kit comprising, in at least a first suitable container, at least a first nucleic acid segment and a structural matrix, wherein at least a portion of said structural matrix is a structural, porous modified alginate matrix that comprises at least one alginate chain section bonded to at least one molecule that mediates cellular interactions or a structural matrix comprised of a porous, synthetic polymer that contains pores formed by gas foaming and pores formed by leaching out of a particulate from the polymer.

67. (Original) The kit of claim 66, wherein said at least a first nucleic acid segment and said structural matrix are physically associated within a single container.

68. (Previously Presented) An implantable device comprising at least a first nucleic acid segment in association with a structural matrix, wherein at least a portion of said structural matrix is a structural, porous modified alginate matrix that comprises at least one alginate chain section bonded to at least one molecule that mediates cellular interactions or a structural matrix comprised of a porous, synthetic polymer that contains pores formed by gas foaming and pores formed by leaching out of a particulate from the polymer.

102. (Previously Presented) The kit of claim 66, wherein at least a portion of said structural matrix is comprised of a porous, synthetic polymer that contains pores formed by gas foaming and pores formed by leaching out of a particulate from the polymer.

103. (Previously Presented) The implantable device of claim 68, wherein at least a portion of said structural matrix is comprised of a porous, synthetic polymer that contains pores formed by gas foaming and pores formed by leaching out of a particulate from the polymer.

104. (Previously Presented) A composition comprising at least a first nucleic acid segment in association with a structural matrix, wherein:

- (a) at least a portion of said structural matrix is comprised of a porous polymer that contains pores formed by gas foaming and pores formed by leaching out of a particulate from the polymer; or
- (b) at least a portion of said structural matrix is a porous alginate or modified alginate matrix;

and wherein said nucleic acid segment encodes a protein or polypeptide that stimulates a bone progenitor cell, wound healing fibroblast, granulation tissue fibroblast or repair cell when expressed in said cell, or that stimulates an immune response when expressed by an antigen presenting cell, or that induces cell death upon expression in a cell.

105. (Previously Presented) A composition comprising at least a first nucleic acid segment in association with a structural matrix, wherein:

- (a) at least a portion of said structural matrix is comprised of a porous polymer that contains pores formed by gas foaming and pores formed by leaching out of a particulate from the polymer; or
- (b) at least a portion of said structural matrix is a porous alginate or modified alginate matrix;

and wherein said nucleic acid segment encodes a transcription or elongation factor, cell cycle control protein, kinase, phosphatase, DNA repair protein, oncogene, tumor suppressor, angiogenic protein, anti-angiogenic protein, immune response stimulating protein, cell surface receptor, accessory signaling molecule, transport protein, enzyme, anti-bacterial protein or polypeptide, anti-viral protein or polypeptide, hormone, neurotransmitter, growth factor, growth factor receptor, interferon, interleukin, chemokine, cytokine, colony stimulating factor or chemotactic factor protein or polypeptide.

106. (Currently Amended) The composition of claim ~~105~~ 125, wherein said nucleic acid segment encodes a growth hormone (GH) protein or polypeptide, a parathyroid hormone (PTH) protein or polypeptide, a PTH1-34 polypeptide or a bone morphogenetic protein (BMP) protein or polypeptide.

107. (Previously Presented) The composition of claim 106, wherein said nucleic acid segment encodes a BMP-2A, BMP-2B, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7 or BMP-8 protein or polypeptide.

108. (Currently Amended) The composition of claim ~~105~~ 125, wherein said nucleic acid segment encodes a transforming growth factor- α (TGF- α), TGF- β 1 or TGF- β 2 protein or

polypeptide, a latent TGF β binding protein (LTBP) protein or polypeptide, an activin/inhibin protein or polypeptide, a fibroblast growth factor (FGF), a granulocyte/macrophage colony stimulating factor (GMCSF), an epidermal growth factor (EGF), a platelet derived growth factor (PDGF), an insulin-like growth factor (IGF) or a leukemia inhibitory factor (LIF).

109. (Previously Presented) A composition comprising at least a first nucleic acid segment in association with a structural matrix, wherein:

- (a) at least a portion of said structural matrix is comprised of a porous polymer that contains pores formed by gas foaming and pores formed by leaching out of a particulate from the polymer; or
- (b) at least a portion of said structural matrix is a porous alginate or modified alginate matrix;

and wherein said composition further comprising a population of cells.

110. (Previously Presented) The composition of claim 109, wherein at least a portion of said nucleic acid segment is taken up by the cells comprised within said composition.

111. (Previously Presented) A composition comprising at least a first nucleic acid segment in association with a structural matrix, wherein at least a portion of said structural matrix is comprised of a porous polymer that contains pores formed by gas foaming and pores formed by leaching out of a particulate from the polymer; and wherein the polymer in said portion of said structural matrix is a lactic acid polymer, glycolic acid polymer or lactic acid/glycolic acid copolymer.

112. (Previously Presented) The composition of claim 111, wherein at least a portion of said structural matrix is comprised of a lactic acid/glycolic acid (PLGA) copolymer matrix.

113. (Previously Presented) A structural matrix-nucleic acid composition comprising at least a first nucleic acid segment in association with a structural matrix that has an interconnected or open pore structure, wherein:

- (a) at least a portion of said structural matrix is comprised of a porous polymer that contains pores formed by gas foaming and pores formed by leaching out of a particulate from the polymer; or
- (b) at least a portion of said structural matrix is a porous alginate or modified alginate matrix;

and wherein said structural matrix-nucleic acid composition promotes proliferation, migration, ingrowth or infiltration of cells into said structural matrix and wherein said cells take up and express said nucleic acid segment.

114. (Previously Presented) The composition of claim 2, wherein at least a portion of said structural matrix is comprised of a polyester, polyanhydride, polyphosphazine, poly(vinyl alcohol), poly(alkylene oxide), poly(allylamine), poly(acrylate), modified polystyrene or polyolefin polymer or copolymer.

115. (Previously Presented) The composition of claim 114, wherein at least a portion of said structural matrix is comprised of a polyhydroxybutyrate, poly- ϵ -caprolactone, poly(ethylene oxides), poly(4-aminomethylstyrene), poly(vinylpyrrolidone), polyethylene, polypropylene or polyethylene terephthalate polymer or copolymer.

116. (Previously Presented) A structural matrix-nucleic acid composition comprising at least a first nucleic acid segment in association with a structural matrix that has an interconnected or open pore structure, wherein:

- (a) at least a portion of said structural matrix is comprised of a porous, synthetic polymer that contains pores formed by gas foaming and pores formed by leaching out of a particulate from the polymer; wherein said synthetic polymer is a lactic acid, glycolic acid, lactic acid/glycolic acid, polyester, polyanhydride, polyphosphazine, poly(vinyl alcohol), poly(alkylene oxide), poly(allylamine), poly(acrylate), modified polystyrene or polyolefin polymer or copolymer; or
- (b) at least a portion of said structural matrix is a porous, modified alginate matrix that comprises at least one alginate chain section bonded to at least one molecule that mediates cellular interactions;

and wherein said structural matrix-nucleic acid composition promotes proliferation, migration, ingrowth or infiltration of cells into said structural matrix and wherein said cells take up and express said nucleic acid segment.

117. (Previously Presented) The composition of claim 116, wherein said synthetic polymer is a lactic acid/glycolic acid (PLGA) copolymer matrix.

118. (New) The composition of claim 48, wherein said nucleic acid segment is a DNA molecule, an antisense nucleic acid molecule or a ribozyme.

119. (New) The composition of claim 48, wherein said nucleic acid segment is comprised within a plasmid or a recombinant expression vector.

120. (New) The composition of claim 48, wherein said nucleic acid segment encodes a marker protein.

121. (New) The composition of claim 48, wherein said nucleic acid segment encodes a protein or polypeptide that stimulates a bone progenitor cell when expressed in said cell.

122. (New) The composition of claim 48, wherein said nucleic acid segment encodes a protein or polypeptide that stimulates a wound healing fibroblast, granulation tissue fibroblast or repair cell when expressed in said cell.

123. (New) The composition of claim 48, wherein said nucleic acid segment encodes an antigenic or immunogenic protein or polypeptide that stimulates an immune response when expressed by an antigen presenting cell.

124. (New) The composition of claim 48, wherein said nucleic acid segment encodes a cytotoxic or apoptosis-inducing protein or polypeptide that induces cell death upon expression in a cell.

125. (New) The composition of claim 48, wherein said nucleic acid segment encodes a transcription or elongation factor, cell cycle control protein, kinase, phosphatase, DNA repair protein, oncogene, tumor suppressor, angiogenic protein, anti-angiogenic protein, immune

response stimulating protein, cell surface receptor, accessory signaling molecule, transport protein, enzyme, anti-bacterial or anti-viral protein or polypeptide, hormone, neurotransmitter, growth factor, growth factor receptor, interferon, interleukin, chemokine, cytokine, colony stimulating factor or chemotactic factor protein or polypeptide.

126. (New) The composition of claim 48, wherein said nucleic acid segment encodes a human protein or polypeptide.

127. (New) The composition of claim 48, comprising at least a first and second nucleic acid segment.

128. (New) The composition of claim 48, comprising a plurality of nucleic acid segments.

129. (New) The composition of claim 48, further comprising a population of cells.

130. (New) The composition of claim 129, wherein at least a portion of said nucleic acid segment is taken up by the cells comprised within said composition.

131. (New) A structural matrix-nucleic acid composition comprising at least a first nucleic acid segment in association with a structural matrix, wherein:

- (a) at least a portion of said structural matrix is comprised of a porous polymer that contains pores formed by gas foaming and pores formed by leaching out of a particulate from the polymer; or

- (b) at least a portion of said structural matrix is a porous alginate or modified alginate matrix;

and wherein said structural matrix-nucleic acid composition is substantially free from residues of organic solvents.

132. (New) A structural matrix-nucleic acid composition comprising at least a first bioactive nucleic acid in association with a structural matrix, wherein:

- (a) at least a portion of said structural matrix is comprised of a porous polymer that contains pores formed by gas foaming and pores formed by leaching out of a particulate from the polymer; or
- (b) at least a portion of said structural matrix is a porous alginate or modified alginate matrix;

and wherein said at least a first bioactive nucleic acid is expressed in a cell upon contact of said structural matrix-nucleic acid composition with said cell.